

### REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-25 are in this case. Claims 15-25 have been withdrawn from consideration. Claims 1-14 were rejected. While continuing to traverse the Examiner's rejections, and without in any way prejudicing the patentability of the rejected claims, the Applicant has, in order to expedite the prosecution, chosen to amend the claims thereby rendering moot Examiner's rejections. Claims 1-14 are canceled herein without prejudice and substituted with new claims 26-45.

#### **Amendments to the Specification**

The Applicant wishes to correct a minor error that occurred in the specification. Particularly, the word "layer" is removed, and the word "average" thickness was added, because as a point of fact the amount gold deposited on the carbon electrode, as disclosed, is insufficient to form a layer.

#### **Rejections under 35 U.S.C § 102(b)**

Claims 1,6 and 10 were rejected under 35 U.S.C 102(b) as being anticipated by Wang et al. (Analytic Chimica Acta, 361,1998, pp. 85-91, hereinafter Wang-1)

Claims 1-3, 6, 10, 12 and 13 were rejected under 35 U.S.C. 102(b) as being anticipated by Naal et al. (Analytical Chemistry 2002, 74, pp. 140-148, hereinafter Naal)

Claims 1-4,6 and 10 were rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. (Analyst, 2000, 125, pp. 1453-1457, hereinafter Xu)

Claims 1-3,5,10, and 12 were rejected under 35 U.S.C. 102(b) as being anticipated by Ye ( Analytical Chemistry, 1988, 60, 00. 1979-1980, hereinafter Ye)

**The References and Differences of the Present Invention Thereover:**

Prior to discussing the claims, Applicant will first discuss the references of the prior art of record and the novelty of the present invention and its unobviousness over the references.

Wang-1 discloses an electrochemical sensor for remote continuous monitoring of TNT using a carbon fiber working electrode assembly. Wang discloses on page 86, section 2.1 use of 6M nitric acid. Examiner speculates (para. 8 ) that the nitric acid soaking results in a chemical modification of the electrode surface. Applicant respectfully submits that use of nitric acid is *only* for cleaning the electrode and does not result in electrode surface modification. As evidence, in presence of nitric acid, the peak current (as shown in Fig. 3 of Wang-1) is expected to appear between 0.0-0.1V because peak current potential depends on pH according to the Nernst equation; whereas Wang-1 discloses peak current at -0.5V in a phosphate buffer (pH=7.4) indicating that nitric acid is not present. Parenthetically, both Xu and Ye disclose cleaning of the electrode with nitric acid.

Conducting polymer films are used in electro-analytical chemistry. Naal, Xu and Ye disclose electro-chemical techniques based on conducting polymer films (CPF): poly-pyrrol-bipyridine, poly-phenylene-diamine (PPDA), and poly-aniline (PA).

Xu and Ye disclose conducting polymer films based on PPDA and PA. Naal discloses conducting polymer films, and fusion with another mediator (which is not stable and expensive) a nitro-reductase maltose binding protein.

By way of introduction, Applicant respectfully affirms that there is a fundamental difference between the present invention and the disclosures of Naal, Xu and Ye and other chemists who work with polymer films.

The present invention works with surface modification by monomers in monomeric solutions, not surface modification by polymerization on the surface. Note that it is well known that after polymerization, monomer traces are carefully removed, for instance Naal p.143, col 1, paragraph 3, "*modified electrode was rinsed thoroughly with acetone and water*"). Conducting polymer films require a proton for conductivity, i.e. acid or neutral background electrolyte and consequently polymer films work in the anode range (see, for example: Hong, J.Phys. Chem. B 2005, 109, 9305-9310, Fig. 1 and Han, J. Phys. Chem. B 2004, 108, 13921-13927, p.13927 and

abstract both attached to the present response). In background solutions with  $\text{pH} > 8$  conductivity of conducting polymer films is decreased and nearly absent for all practical purposes.

Specifically, Xu prepared from phenylene-diamine monomer solutions a conducting polymer film poly-0-phenylenediamine (PPDA). It is well known by Xu and other researchers in this field that PPDA film as practically all conducting polymer films have high conductivity in presence of a proton, i.e. in acidic medium. This is the reason Xu works with malic acid as background electrolyte. Xu PPDA polymer film includes ternary aminogroups (p.1454, scheme 1, C) is not specifically selective to nitro-aromatic, but also to  $\text{NO}_3^-$  anions. Xu shows (Fig.2) that the same potential  $-0.05 \text{ V}$  relates to all anions. This is a consequence of electronic conductivity of conducting polymers, instead of ionic conductivity of monomers. Applicant suggests this as a reason for a low detection limit (DL) in Xu (about  $2\text{-}5 \mu\text{M/l}$  ( $\sim 200\text{-}500 \text{ ppb}$ ), p.1456, table 1).

Ye prepared Pt/poly-aniline (Pt/PAN) electrode. The Pt/PAN electrode is suitable for anion detection in acid solutions because of low over potential hydrogen evaluation on Pt. However Pt and also Pt/ PAN cannot work in cathode range (especially at  $\text{pH} > 8$ ) and cannot be used to detect nitro-aromatic compounds.

In contrast, in the present invention, nitro-aromatic reduction current increases with increasing pH. This is evident from the progression of experimental results : sensitivity  $S = \Delta I / \Delta C$  (microampere/ppb) is measured at  $0.003 \text{ microampere/ppb}$  at  $\text{pH}=4$  (page 8, line 18) and sensitivity is  $0.66 \text{ mA/ppb}$  at  $\text{pH}=9$  (page 10, line 2), and shown in Figures 3 and 6. Consequently, high  $\text{pH} > 8$  is required for high sensitivity and the present invention works in the cathode range. Applicant submits that any even minimal increase in measured sensitivity as shown by Naal, Xu, Ye or any other chemists, cannot be due to the chemical mechanism as disclosed in the present invention. Operation in the cathode range at high pH causes the increased (e.g. TNT) detection sensitivity  $S$  in the present invention from  $0.001 \text{ microampere/ppb}$  (Naal, fig. 7 inset) and  $0.0005 \text{ microampere/ppb}$  (Wang-1, fig. 5a) to  $0.66 \text{ mA/ppb}$  (Fig. 6 PP) i.e. in 660 times to Naal and in 1320 times to Wang-1.

Furthermore, the Applicant wishes to point out that the present invention is based on a chemical analogy to a Meisenheimer type complex that occurs on the electrode surface only as a monomer. According to Meisenheimer, a nitro-aromatic compound forms a complex with a monomeric primary amino-aromatic compound, *e.g.* aniline bound by Van Der Waals force to the surface of the electrode, when dissolved in an aprotic solvent. The Meisenheimer type complex does not occur with a polymeric amine, such as in poly-aniline because in the polymer the amine is relatively inactive.

#### **Independent Claims 26 and 45**

New independent claims 26 (rewritten from claim 1) and claim 45 include novel physical features or steps. Specifically, independent claim 26 and 45 include a limitation, *"a working electrode having a surface.. modified by a monomeric amino-aromatic compound by treatment thereof with said monomeric amino-aromatic compound dissolved in an organic polar solvent"*

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)

Wang-1 discloses cleaning of an electrode with nitric acid, prior to use, and as previously discussed does not perform any surface modification of the electrode with or without an organic polar solvent.

Naal discloses electropolymerization of poly-pyrrol-bipyridine (PPB) on an electrode. Applicant respectfully traverses Examiner's (paragraph 13) that the chemical modifier includes an amino-aromatic compound. In fact, both pyrrol and bipyridine are heterocyclic and not aromatic. Further, Naal is not performing surface modification by a *monomeric amino-aromatic* compound, but electropolymerization on the surface of an electrode.

Xu discloses electropolymerization as a thin film of o-phenylenediamine on a gold electrode. Further Xu discloses electropolymerization in an *inorganic* solution, specifically 1.0 mol/L sulfuric acid. Hence, Xu does not disclose *"a surface modified*

*by a monomeric amino-aromatic compound by treatment thereof with said monomeric amino-aromatic compound dissolved in an organic polar solvent".*

Ye discloses electropolymerization of polyaniline films on a platinum electrode in an *inorganic* solution, 1.0 M sulfuric acid. Hence, Ye does not disclose *"a surface modified by a monomeric amino-aromatic compound by treatment thereof with said monomeric amino-aromatic compound dissolved in an organic polar solvent"*.

### **Rejections under 35 U.S.C § 103**

Although Applicant submits that new independent claims 26 and 45 are patentable, thereby rendering claims dependent therefrom patentable as well, the Applicant wishes to briefly comment regarding the dependent claims.

Claim 6 was rejected under 35 U.S.C § 103(a) as being unpatentable over Ye in view of Xu. As previously discussed, Ye or Xu disclose electropolymerization in inorganic acid aqueous solutions which is very different from surface modification by a monomer in an organic polar solvent. Consequently, any combination of Yu, Xe or any other similar references in the field of electropolymerization would not render the present invention obvious to "one skilled in the art".

Claims 6,7, and 9 were rejected under 35 U.S.C § 103(a) as being unpatentable over different combinations of Ye, or Xu with Shi et al. (US patent 6,356,433), or Ko et al. (US patent 4,895,620).

Shi teaches *bare* carbon paper for preparation of ultra-capacitors. For the ultra-capacitors a high surface area is required to maximize capacitance. (Shi column 1, line 60), In the present invention, high surface area is detrimental and gives rise to enormous background current. Hence, in embodiments of the present invention, gold is deposited on the *bare* carbon electrode to reduce the surface area (dependent claim 35), and treatment in a aprotic solvent, (*e.g.* dimethylsulfoxide) reduces the effective surface area of the *bare* carbon electrode thereby reducing the background current.(dependent claims 30 and 31). Furthermore, Applicant submits based on his own experimentation, that application of the teachings similar to Ye with use of bare carbon paper, does not obtain satisfactory background current with bare carbon paper.

Hence, without applying the teachings of the present invention to reduce background current, combination of any of the prior art references on record with Shi leads to an *inoperable* combination.

Ko teaches a method for preparing electrically conductive carbon-coated fibers. Example 1 (col. 8) teaches a mix of carbon powder with unbleached soft wood-pulp as an insulator. The anisotropic composite material is intended for use as an antistatic material. In example 3 Ko prepared a mixture from carbon powder and newspaper: From Ko (col.11, line 20) "...the newspaper (in pulp form) was mixed together with the carbon powder" . Surface average resistivity in materials prepared by Ko is from  $10^{12}$  (table 1) to  $10^3$  ohms/sq (table 3). For a working electrode useful in electrochemistry, not only according to the present invention, a much lower surface resistivity is required, at least 3-5 ohms/sq. Applicant respectfully traverses Examiner's statement in paragraph 27 of the present communication indicating that the teachings of Ko lead to "low surface resistivity". Applicant further submits that according to his chemical experience, materials prepared according to the teachings of Ko are not useful as a working electrode in electrochemical trace analysis, because indefinite impurities in, for instance wood pulp and newspaper, will misrepresent voltammetric curves, especially with use of organic solvents. Hence, for any of these reasons, a combination of the teachings of Ko with any other of the prior art references on record is *inoperable*.

Claims 7 and 9 were rejected under 35 U.S.C § 103(a) as being unpatentable over Wang-1 or Naal in view of Bennetto et al. (US patent 4,970145)

Bennetto teaches a method of preparation of an enzyme electrode enzyme electrode or biosensor including an enzyme immobilised on the surface of an electrically conducting support member. The support member includes a porous layer of resin-bonded carbon or graphite particles. The particles are intimately mixed with a finely divided platinum group metal, to form a porous, substrate layer (*e.g.* Pt black) onto which the enzyme is adsorbed.

. It is well known that Pt black, is suitable for operation only in the anode range in aqueous solutions (Bennetto, Fig1.  $E_p = + 600$  mV). Additionally, a Pt black based electrode with optimally a large effective surface area can not work in voltammetric regime, because of high background current. Thus, Bennetto uses chronoamperometry and not voltammetry. Pt black, can not work in the cathode range, because of a low hydrogen evolution over-potential (ie. a small cathode

window). The present invention, uses for instance modified carbon paper electrode with a cathode window to -1.5 V (vs Ag/AgCl) and  $E_p = -600$  mV. Hence, an average chemist would not attempt combining the teachings of Bennetto with other references to achieve the present invention because of inherent *inoperability*.

Claim 8 was rejected under 35 U.S.C § 103(a) as being unpatentable over Xu in view of Glass (US patent 5,296,125). Glass discloses electrodes including gold layers on chromium (col 14, lines 45-50) for explosives detection in an organic background electrolyte. It is also well known that in electrodes of this type that chromium being an electro-active metal, the gold is required to be a thick layer of at least one micrometer. Otherwise chromium will dissolve in the electrolyte and the chromium reduction current will be too high, especially in the presence of water.

The present invention uses gold deposited on carbon paper in a non-contiguous "layer" or more exactly islands of average thickness less than one nanometer. The presence of gold as a surface modifier decreases the effective area of the active surface and reduces the background current. New dependent claim 35 (amended form of claim 8) reflects this distinction.

Claims 12 and 13 (re-presented in amended form as claims 39 and 40) were rejected as being unpatentable over Wang-1 in view of Wang et al. (Analytical Chemistry, 2002, 74, pp. 1187-1191, hereinafter Wang-2) Examiner notes in paragraph 43 of the present communication: "Wang-2 discloses that it is conventional to dissolve TNT in acetonitrile". Applicant agrees with the Examiner that stock solutions of TNT in acetonitrile are conventional. Wang obtained the TNT solutions in acetonitrile from Radian International (Austin TX). (Wang-2 pg, 1188 col. 2). However, there is a difference between the stock solution which is only a reagent as purchased and the background electrolyte which is part of the invention. Background electrolyte composition is very important because the background electrolyte influences sensitivity. For example, Wang-1 uses as electrolyte of 0.01 M phosphate buffer (p.87, Fig.1) in combination with bare carbon. Wang -2 discloses a more complicated buffer: 15 mM phosphate buffer + 20mM Na-dodecyl sulphate (SDS) and 2-(4-morpholino) ethane-sulphonic acid hydrate (MES) + 10mM SDS (p.1188-9) for significantly improved separation of different 6 explosives peaks on bare carbon electrode.

But in this case Wang-2 lost sensitivity;  $S = 1 \times 10^{-6}$   $\mu\text{A/ppb}$  (Fig. 3A, p/1189 Wang-2).

Applicant experimentally found combination of mixed background and modified electrode increases sensitivity S to 0.66  $\mu\text{A/ppb}$ .

Claims 14 and claim 10 were rejected under 35 U.S.C § 103(a) as being unpatentable over Wang-1 or Naal in view of Peyton (US patent 5,762,808). Peyton teaches a process for treating aqueous streams contaminated with nitro-aromatic Peyton teaches that DNT readily dissolves in alcohol, and uses such a solution for test purposes. However, Peyton's disclosure is in a different field from the present invention and does not teach or even suggest that mixed ethanol aqueous solutions may be effectively used as a background electrolyte in an electro-chemical assay, hence combination of Peyton with any other references on record is not appropriate.

Furthermore, there is no justification in any of the prior art references of record which suggests that these references should be combined, much less be combined in the manner proposed. It is well known that in order for any prior art references themselves to be validly combined for use in a prior art §103 rejection, *the references themselves* (or some other prior art) must suggest they are combined, as stated in *e.g.* re Sernaker 217 U.S.P.Q. 1,6 (C.A.F.C 1983):

“Prior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantages to be derived from combining their teachings”.

In line with this decision, the Board stated in *Ex parte Levengood* 28, U.S.P.Q.2d 1300 (P.T.O.B.A&I. 1993):

“In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*, preferably in the form of some teaching, suggestion, incentive or inference in the applied art, or in the form of generally available knowledge”

Applicant respectfully submits that combination of the prior art references is not appropriate based on the arguments presented herein.



**Novel physical features of Independent claims 26 and 45**

**Produce New and Unexpected Results**

The present invention which includes a surface *"modified by a monomeric amino-aromatic compound by treatment thereof with said monomeric amino-aromatic compound dissolved in an organic polar solvent"* produces an electro-chemical assay with new and unexpected results.

In particular, in the present invention, the modification of the surface of the working electrode, separates the oxygen background signal from signal from the nitro-aromatic compounds, *e.g.* TNT under assay, (Figure 1 ) allowing the sensitivity of the assay to be high even in the presence of oxygen. Further modification such as by using minute gold deposition on the carbon surface, further separates the oxygen signal from the TNT signal.

The present invention works in the presence of oxygen and can even use an air inlet (dependent claim 11 re-presented as claim 38) to measure trace nitro-aromatic compounds in the present even in air. In comparison, Naal, teaches that the cell must be hermetic (p.142, col. 2 under Instrumentation) because oxygen destroys the measurement.

Further to these remarks is attached a declaration under 37 CFR 1.132 which includes evidence as to the separation of the TNT peak and the oxygen peak.

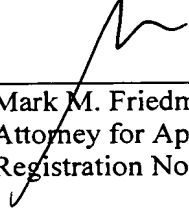
Sensitivity of the present invention, further improved by the use of the mixed electrolyte reaches very high levels 0.66 microampere /ppb. (page 10, line 3)

In comparison, measurement sensitivity of Naal is 0.001 microampere/ppb (Naal, fig. 7 inset) and that of Wang 0.0005 microampere/ppb (Wang-1, fig. 5a) Glass reported (p.11, example 1) the test concentrations of TNT are 2.5 mM. (The concentration of TNT is ~ 660 mg/l (ppm), i.e. more than 100,000 times higher (less sensitive) than the trace analysis as measured in parts per billion in the present invention.

The new claims are fully supported by the specification and new matter has not been added in the present amendment.

In view of the above amendments and remarks it is respectfully submitted that independent claims 26 and 45 and claims dependent therefrom are in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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